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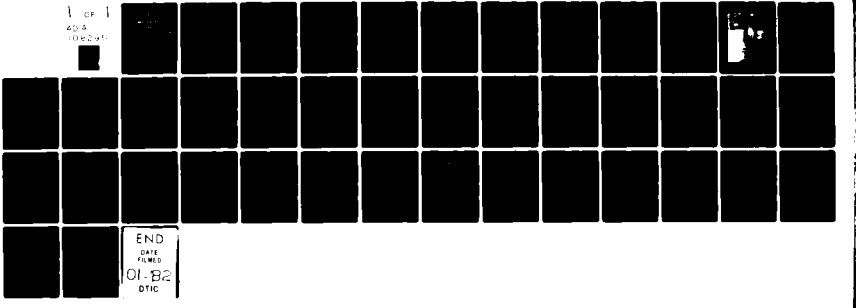

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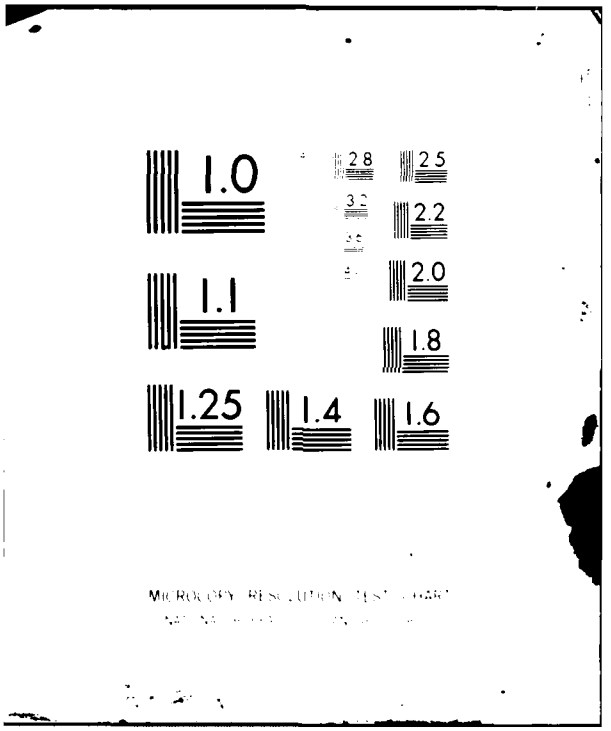
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LEVEL II

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Report Number One

ASSESSMENT OF ANTIRADIATION DRUG EFFECTIVENESS TO FISSION NEUTRON IRRADIATION

ANNUAL REPORT

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SUMMARY

This report deals with the assays of various compounds for their toxicity of anti-radiation efficacy following exposure to either Co-60 or fission neutron irradiation. The compounds reported herein include WR 347, WR 2721, WR 3689, WR 44923, WR 109342, WR 151327, WR 16843, and WR 176542. The endpoints measured in the radiation studies were LD50(6) and LD50(30).

The compounds and their dose modification factors (DMF) for the neutron LD50(6) following i.p. administration, were, in descending order of effectiveness: WR 151327 (1.42), WR 347 (1.37), WR 3689 (1.34) WR 44923 (1.34), WR 2721 (1.26), WR 168643 (1.24), and WR 176542 (1.23). The corresponding LD50(30)'s for fission neutron irradiation following i.p. administration, were: WR 168643 (1.67), WR 3689 (1.52), WR 151327 (1.45), WR 44923 (1.39), WR 347 (1.22), WR 2721 (1.21), and WR 176542 (1.18).

For low LET Co-60 gamma irradiation the LD50(6) and LD50(30) were determined for WR 347 following i.p. administration. The DMF's obtained were: LD50(6) (1.4), LD50(30) (1.5).

FOREWORD

In conducting the research described in this report, the investigator(s) adhered to the "guide for the Care and Use of Laboratory Animals," prepared by the Committee on Care and Use of Laboratory Animals of the Institute of Laboratory Animals Resources, National Research Council (DHEW Publication No. 78-23, Revised 1978).

It should be noted that this Annual Report presents data which has been generated only in the first four-and-one-half months of the scheduled one-year contract and does not represent an entire year's work. Experiments needed to fulfill the first year's contractual obligations are continuing.

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INTRODUCTION

The efficacy of sulphydryl compounds as radioprotective agents was first demonstrated by Patt in 1949 (1). Subsequent to these studies, many compounds have been tested for their ability to protect against the effects of ionizing radiation. The decarboxylated cysteine derivative, cysteamine (mercaptoethylamine, MEA, WR 347) was found to be the best protector in the sulphydryl class, giving dose reduction factors (DRF) of approximately 1.3 for intestinal death (2) and 1.8 for hematopoietic death (3). In 1959 Akerfeldt (4) reported the synthesis of a thiophosphate derivative of cysteamine which was characterized by a phosphate group covering the sulphydryl. These phosphorothiotic acids were shown to provide significant increases in radioprotection as compared to the compounds containing sulphydryl groups alone (5,6). Further synthesis and screening of phosphorothiotic acids demonstrated the most effective radioprotector to be WR 2721 (7). It is not only less toxic than cysteamine (8), but it also protects irradiated skin and bone marrow preferentially over tumor (9) and provides differential protection in several other normal tissue-tumor systems (10,11,12,13). However, there are problems of toxicity and less than adequate protection of some dose-limiting critical organs, such as kidney, lung, and central nervous system (8,14).

More recently, other phosphorothiotic compounds have been synthesized which may provide either decreased toxicity or increased protection as compared to WR 2721. Some of these drugs, such as cysteamine phosphate (WR 638) and WR 77913 have shown radioprotection comparable to that of WR 2721 in the small intestine (2,15,16). Davidson (17) has recently reported that WR 3689 is better tolerated and has better protective activity in mice than WR 2721. The present study extends the number of thiophosphate compounds investigated as potential radioprotective agents against either Co-60 gamma radiation or fission neutron radiation.

MATERIALS AND METHODS

1. Animals

The animals used in all experiments were male C57/Bl/6 mice (Charles Rivers), 70-77 days of age at the time of exposure to drugs and/or radiation. Prior to beginning any experiment the mice were allowed one week to adapt to the local animal care facility's environmental conditions. They were kept on wood-chip bedding in plastic mouse boxes (28 x 17 x 12.5 cm) with stainless steel wire tops (five animals per box). The mice were maintained on standard mouse chow (Purina) and chlorinated water (15 ppm) ad libitum. The animal room was maintained at 22° C and with a 12/12 hour light-dark cycle (lights on at 0600 hours Eastern Standard Time and lights off at 1800 hours EST).

2. Low LET Radiation

In all low LET irradiation procedures, mice were exposed to whole-body gamma radiation with a cobalt-60 teletherapy unit (Picker C-10000). A 20 x 20 centimeter field was used with a source-to-subject distance (SSD) of 95 centimeters. The dose rate varied slightly from experiment to experiment, due to radioactive decay, but was generally in the 95-100 rads/minute range. An average exposure rate was determined with a thimble chamger and a Victoreen condenser R-meter. A plexiglass container was used to hold the ten mice which were used at each dose level.

3. High LET Radiation

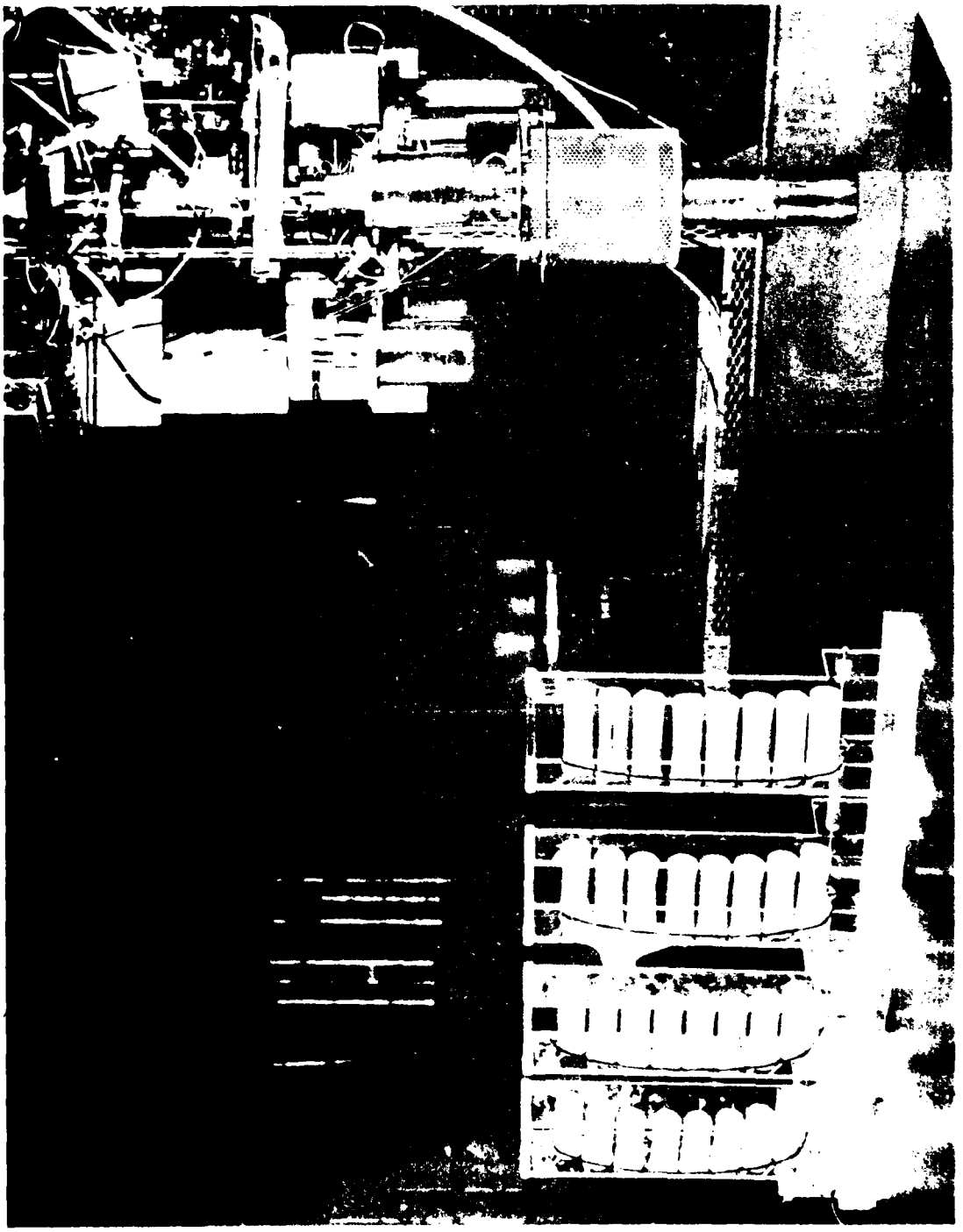
Fission neutron facilities for mouse irradiation were furnished by the Health Physics Reactor (DOSAR) at Oak Ridge National Laboratory. The reactor facility has been described in some detail (18). The fission spectrum has a peak energy of 0.9 MeV with a mean energy of 1.2 MeV. The mice will be irradiated in nylon tubes 2 meters or more from the unshielded core. Fig. 1 shows the irradiation setup. Power level was set at 2 KW with a dose rate of about 30-40 rads/min. Gamma contamination usually amounted to about 15% of the dose for the irradiation protocol. A good discussion of the dose and LET distribution in small animals using this reactor was presented by Willhoit and Jones in 1970 (19). Sigdestad (20) has described the RBE for this radiation procedure. For full details of the irradiation procedures and parameters used in the first two trips to HPRR/ DOSAR see appendices one and two.

4. Radioprotective Compounds

The radioprotective compounds used throughout this investigation were: WR 347, WR 2721, WR 3689, WR 44923, WR 109342, WR 151327, WR 168643, and WR 176542. Pertinent information concerning these drugs is given in Table 1.

Drugs were administered 30 minutes prior to gamma radiation exposure following an i.p. injection and 30-45 minutes prior to neutron irradiation after i.p. administration. The time of drug administration to irradiation was more variable in the neutron radiation due to reactor operation constraints.

Figure 1. Neutron irradiation procedure. The mice are in nylon tubes two meters or more from the reactor.



5. Lethality Experiments - Drugs

Drugs were administered to the mice either intraperitoneally (i.p.) or per os (p.o.). Ten mice per dose group were used and lethalities were recorded for ten days after drug administration, although no deaths occurred later than two days post-injection. The probit analysis method of Finney (21) was used to calculate the lethal drug dose for 50% of the population (the LD50).

6. Lethality Experiments - Radiation

Four to ten mice were used in each radiation dose group. Where 0% or 100% lethal response was expected, fewer numbers of animals were used in order to ensure higher efficiency in numbers of mice used per significantly-weighted data point.

Lethalities were recorded each day for thirty days following radiation exposure and were scored either as LD50(6) (lethalities occurring within the first six days post-irradiation) or LD50(30) (lethalities occurring within 30 days post-irradiation). LD50's were determined using probit analysis.

Intercomparison analyses between control lethalities (non-protected mice) and drug-protected mice were calculated according to the dose-modification factor (DMF). The DMF is defined as the ratio of equally effective radiation doses which are needed to produce an identical radiation response. The DMF's for lethality were calculated at the LD50 value as follows:

$$DMF = \frac{\text{LD50 treated}}{\text{LD50 untreated}}$$

RESULTS AND DISCUSSION

Pertinent toxicity data for the drugs tested are presented in Table 1. This includes the LD50 for i.p. and p.o. administration as mg of drug per kg of animal weight (mg/kg). The dosage of drug used in radiation experiments was generally two-thirds of the toxic LD50 value unless precluded by increased toxicity during the irradiation procedure. If this occurred, subsequent use of the drug was at one-half of the previously determined toxic LD50.

Tables 2 and 3 show the results of the radiation lethality experiments for Co-60 gamma radiation and fission neutron irradiation respectively. Following the tables the results presented in the tables are discussed for each drug separately.

1. Control (Untreated)

The LD50(6) in the control animals for fission neutron irradiation was determined to be 252 rads. This is identical to the value previously reported in a similar study (22). The LD50(30) for fission neutrons was 220 rads. The proximity in values for the LD50(6) and LD50(30) was not unlike the results of earlier studies (23), the ratio of LD50(6) to LD50(30) being 1.15.

The LD50(6) for Co-60 radiation was 1065 rads. This is somewhat lower than the previous study, which used 4 MeV X-rays (22), but can perhaps be accounted for by the fact that female C57Bl/6 mice were used in these experiments instead of the male C57Bl/6 mice used before, there being a significant difference in the radioresponse of mice of the same strain to low LET radiation. There may also be a differential response due to the different energies of the radiation employed. The LD50(30) for Co-60 irradiation was 738 rads and the ratio of LD50(6):LD50(30) was 1.47.

The RBE (relative biological effectiveness) for the LD50(6) was calculated as the ratio of the LD50(6) for X-rays to the LD50(6) for neutrons. This resulted in an RBE of 4.23 for death in the gastrointestinal lethality dose range. A similar calculation for LD50(30) resulted in an RBE of 3.35, which represented death in the hematopoietic syndrome dose range. The phenomenon of a higher RBE for gut death as compared to marrow death, coupled with the low LD50(6): LD50(30) ratio for neutrons suggests a greater sensitivity of the intestine to neutrons than to gamma radiation, a fact which has been alluded to, but not explained, in earlier studies (24). Figures 2 and 3 illustrate the variation of mortality with time for the radiation doses used in both the low LET and high LET radiations.

2. WR 347

WR 347 is the classic radioprotective compound mercaptoethylamine, also known as MEA or cysteamine. It is now a benchmark of comparison in the ascertainment of efficacy of other, newer agents. Therefore, WR 347 was one of the first of the current series of drugs used in this study. Toxicity data

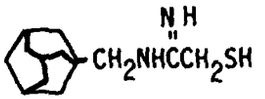
Drug	Structure	Vehicle	LD50 (mg/kg)* i.p.	p.o.
WR 347	$NH_2CH_2\text{-}CH_2\text{-}SH$	H_2O	498 (457-542)	
WR 2721	$NH_2(CH_2)NH(CH_2)_2SPO_3H_2$	H_2O	1108 (1064-1154)	1301 (1135-1491)
WR 3689	$CH_3NH(CH_2)_3NH(CH_2)_2SPO_3H_2$	H_2O	1449 (1378-1525)	1816
WR 44923	$NH_2(CH_2)_3NH(CH_2)_3SPO_3H_2$	H_2O	773 (583-1024)	
WR 109342		H_2O	371 (35.2.39.0)	58.0 (48.6-70.8)
WR 151327	$CH_3NH(CH_2)_3NH(CH_2)_3SPO_3H_2$	H_2O	1011 (983-1039)	
WR 168643	$NaOS(CH_2)_4SSS(CH_2)_4\overset{O}{\overset{\|}{S}}ONa$	H_2O	1272 (1255-1290)	1142
WR 176542	$NH_2(CH_2)_4CHNH_2CH_2SPO_3H_2$	H_2O	649 (629-671)	

TABLE I

Drug Information

*Values in parentheses are 95% confidence limits; where no confidence limits appear the LD50 was estimated by linear regression.

Figure 2. The survival pattern of mice at eight dose levels following Co-60 gamma irradiation.

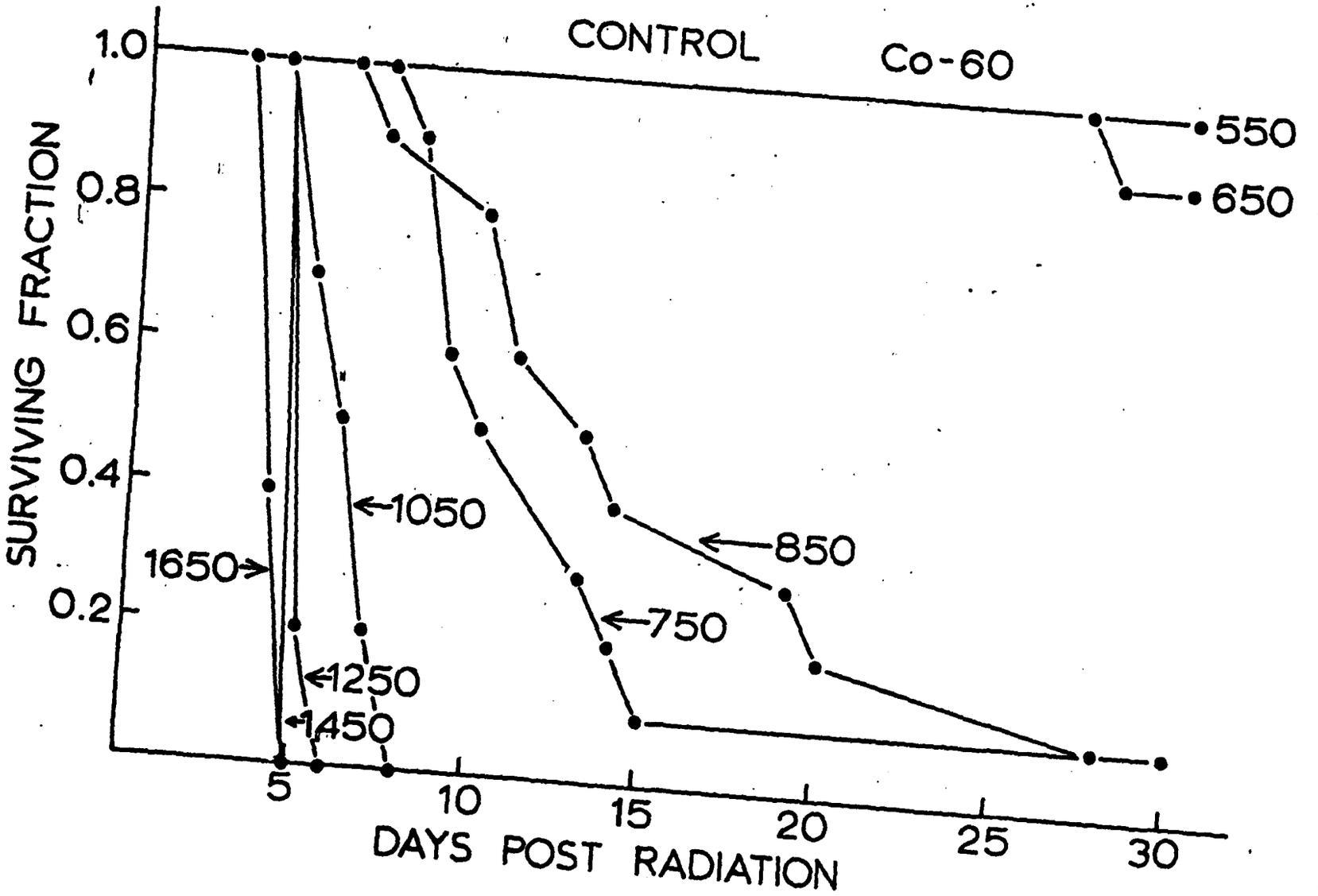
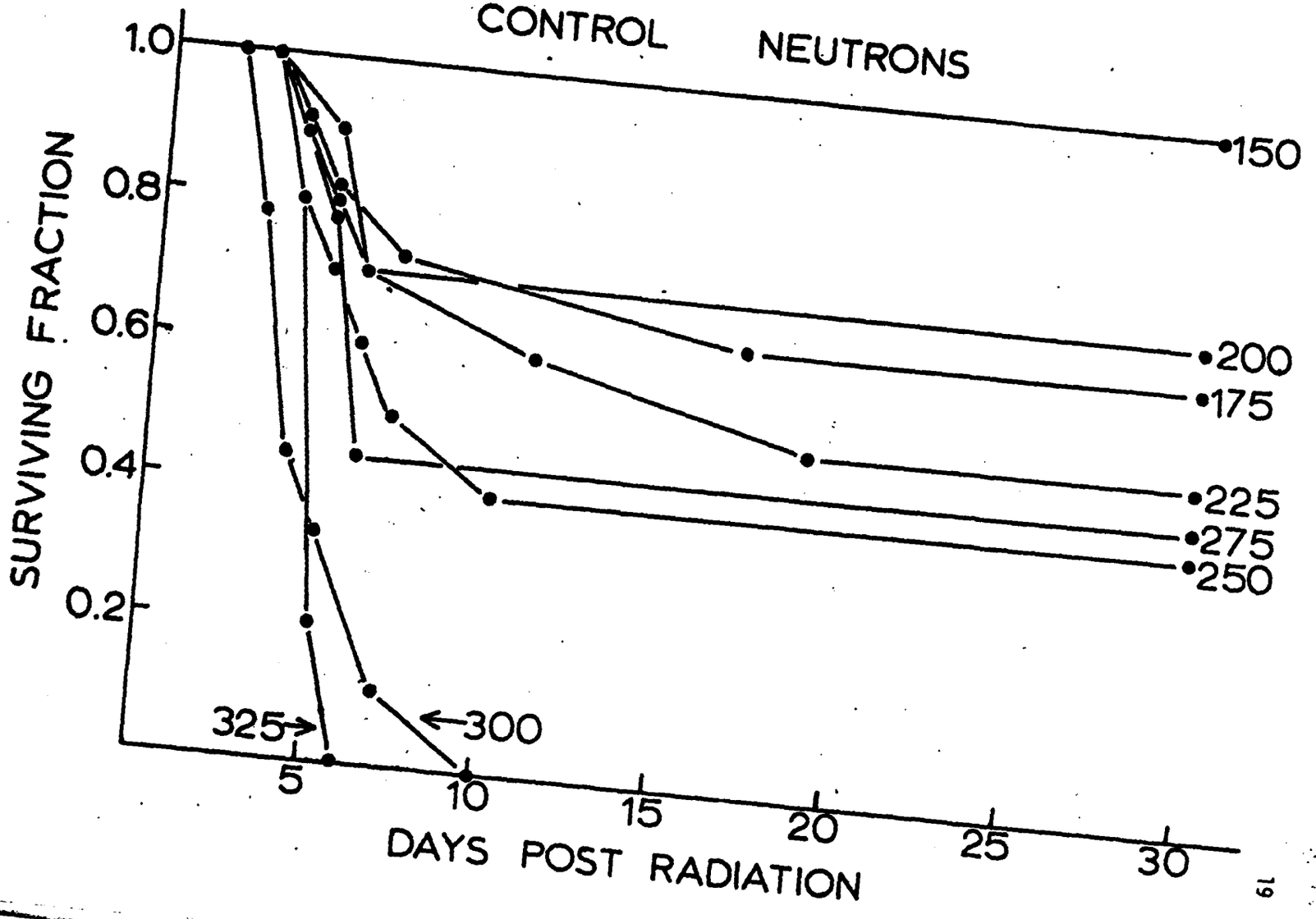

CONTROL
Co-60
550
650
1.0
0.8
0.6
0.4
0.2
SURVIVING FRACTION
1650
1050
850
750
1250
1450
5
10
15
20
25
30
DAYS POST RADIATION

Figure 3. The survival pattern of mice at eight dose levels following fission neutron irradiation.


CONTROL
NEUTRONS
1.0
0.8
0.6
0.4
0.2
SURVIVING FRACTION
150
200
175
225
275
250
325
300
5
10
15
20
25
30
DAYS POST RADIATION

initally showed a LD50 for i.p. injection of 498 mg/kg. When two-thirds of this dose (333 mg/kg was used in theinitial radiation lethality study, approximately 10% mortality resulted. Thereafter a drug dose of 220 mg/kg was used in all studies.

The LD50(6) for gamma irradiation with this drug was 1463 rads, lower than in the previous study, but comparable to the difference observed in the controls (vide supra). This resulted in a DMF of 1.4. The LD50(30) for low LET radiation was 1065 rads, giving a DMF of 1.5. Fission neutron radiation gave a LD50(6) of 350 rads, thus confirming previous results (22) and a LD50(30) of 268 rads. The respective DMF's were 1.39 for gut death and 1.22 for marrow death. In figures 4 and 5 are shown the dose-mortality-time patterns for Co-60 gamma radiation and fission neutron radiation.

3. WR 2721

WR 2721 is a thiophosphate compound which has received extensive study over the last twelve years (25,26) and now is in clinical trails (27). Toxicity studies on this drug showed an i.p. LD50 of 1301 mg/kg. The neutron radiation demonstrated a LD50(6) of 318 rads (DMF=1.26) and a LD50(30) of 267 rads (DMF=1.21) following an i.p. injection of 741 mg/kg. Low LET radiation lethality studies after i.p. or p.o. administration of WR 2721 are in progress.

4. WR 3689

Toxicity testing of WR 3689 resulted in an i.p. LD50 of 1449 mg/kg and a p.o. LD50 of 1816 mg/kg. Irradiation with fission neutrons following an i.p. injection of 970 mg/kg showed the LD50(6) to be 337 rads (DMF=1.33) and the LD50(30) to be 334 rads (DMF=1.52). Figure 6 demonstrates the relationship of dose-mortality to time for this experiment.

5. WR 44923

The drug LD50 from an i.p. injection of WR 44923 was determined to be 773 mg/kg. Two-thirds of this dose (517 mg/kg)was used to obtain neutron lethality data of 337 rads for the LD50(6) (DMF=1.34) and 305 rads for the LD50(30) (DMF=1.39). Currently i.p. LD50(6) and LD50(30) studies on this drug are under way with Co-60 gamma radiation.

6. WR 109342

Toxicity studies showed the i.p. LD50 of WR 109342 to be 37.2 mg/kg and the p.o. LD50 to be 58 mg/kg. At this time LD50(6) and LD50(30) determinations following p.o. administration of this drug before gamma irradiation are in progress.

Figure 4. The survival patterns of mice at eight dose levels following i.p. administration of WR-347 and Co-60 irradiation.

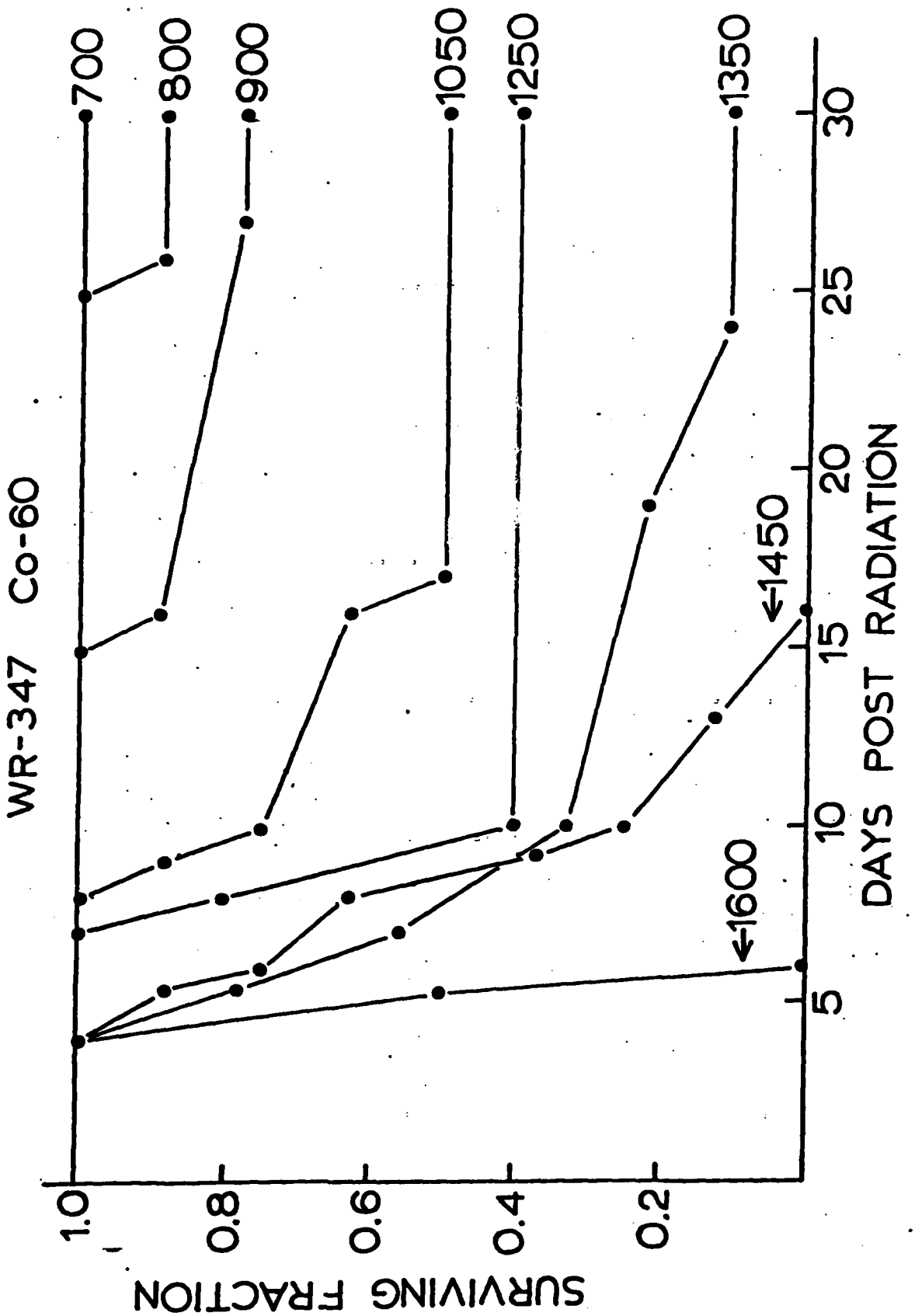

WR-347 Co-60
700
800
900
1050
1250
1350
1450
1600
SURVIVING FRACTION
1.0
0.8
0.6
0.4
0.2
DAYS POST RADIATION
5
10
15
20
25
30

Figure 5. The survival patterns of mice at eight dose levels following i.p. administration of WR-347 and fission neutron irradiation.

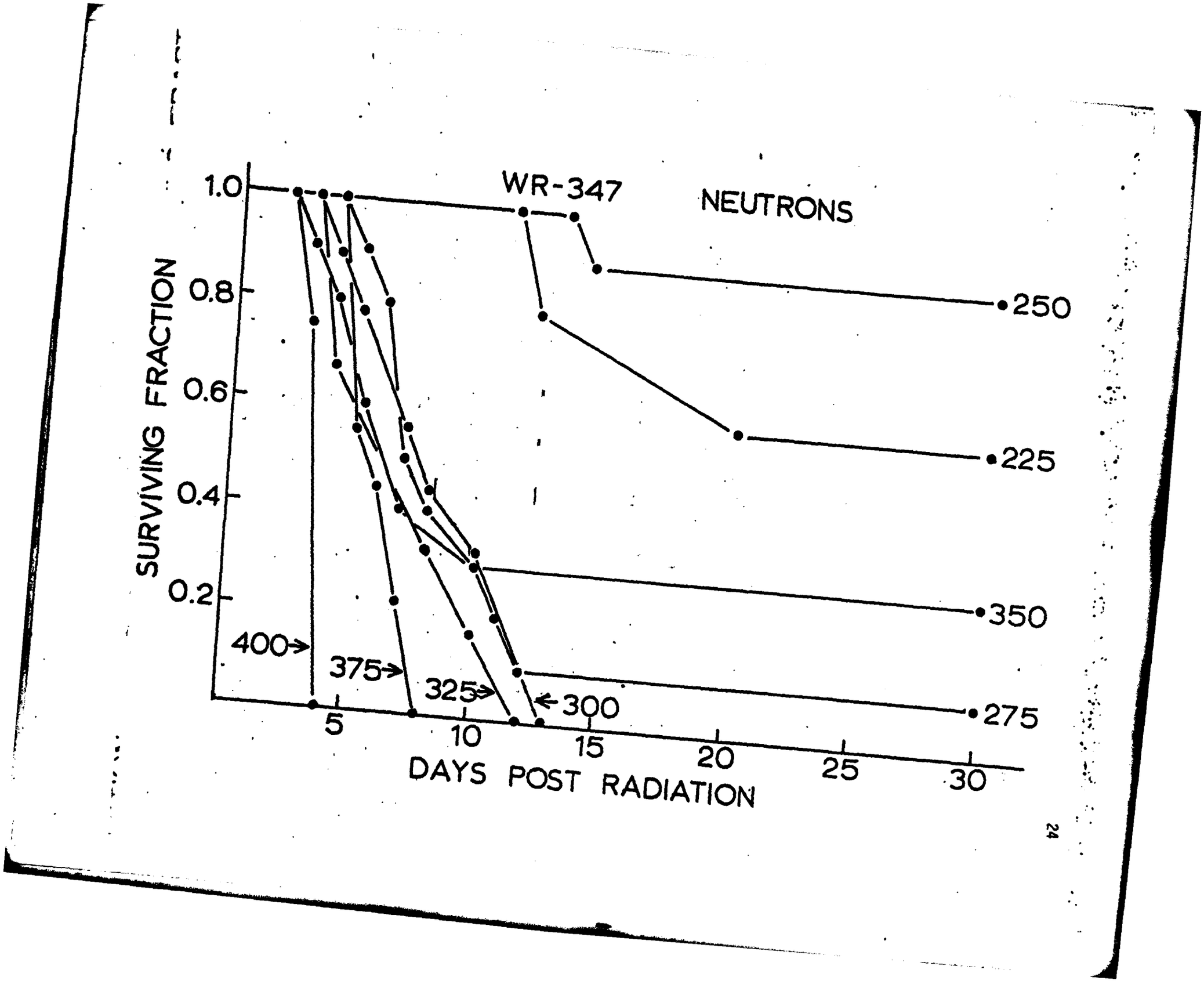
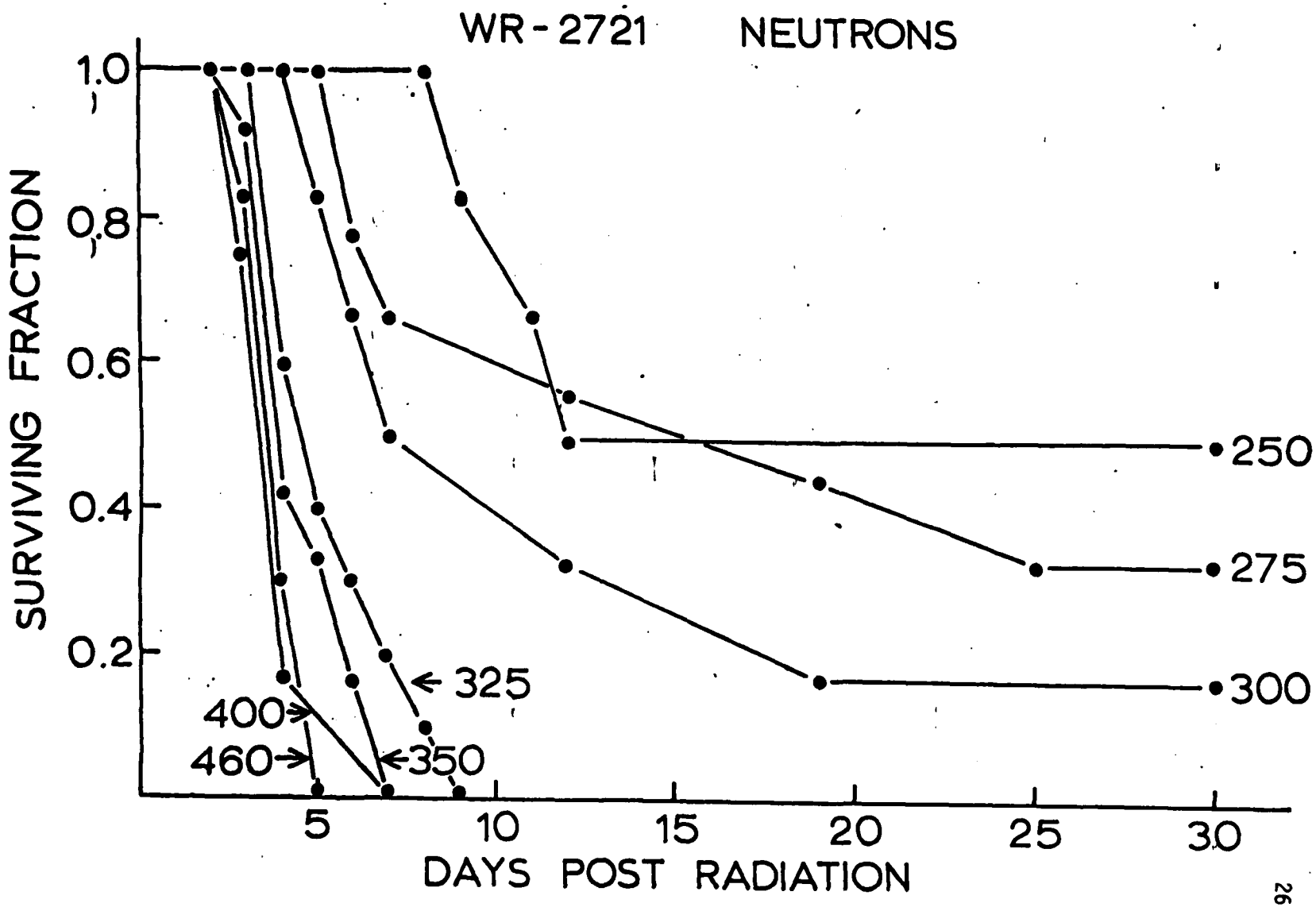

WR-347
NEUTRONS
SURVIVING FRACTION
1.0
0.8
0.6
0.4
0.2
400
375
325
300
250
225
350
275
5
10
15
20
25
30
DAYS POST RADIATION

Figure 6. The survival pattern of mice at seven dose levels following i.p. administration of WR-2721 and fission neutron irradiation.


WR-2721 NEUTRONS
SURVIVING FRACTION
1.0
0.8
0.6
0.4
0.2
250
275
300
325
350
400
460
5
10
15
20
25
30
DAYS POST RADIATION

7. WR 151327

The i.p. LD50 dose of WR 151327 was 1011 mg/kg. An i.p. dose of 677 mg/kg resulted in fission neutron LD50's of 358 rads for 6-day death (DMF=1.42) and 319 rads for 30-day death (DMF=1.45). Low LET lethality studies following an i.p. injection are in progress.

8. WR 168643

The i.p. toxic LD50 for WR 168643 was 1272 mg/kg and the p.o. LD50 was 1142 mg/kg. Following i.p. administration of a dose of 852 mg/kg the neutron LD50's were determined to be 313 rads for the LD50(6) (DMF=1.24) and 267 rads for the LD50(30) (DMF=1.21).

9. WR 176542

This drug gave an i.p. LD50 of 649 mg/kg. The neutron radiation studies, following an i.p. injection of 434 mg/kg resulted in a LD50(6) of 311 rads (DMF=1.23) and a LD50(30) of 260 rads (DMF=1.18). Cobalt-60 i.p. lethality studies are currently under way.

	Dose (mg/kg)		LD50(6) (RADS)		LD50(6) DMF		LD50(30) (RADS)		LD50(30) DMF	
Drug	i.p.	p.o.	i.p.	p.o.	i.p.	p.o.	i.p.	p.o.	i.p.	p.o.
None	--	--	1045 (1017-1074)	--	--	--	710 (692-729)	--	--	--
WR 347	310	--	1463 (1416-1512)	--	1.4	--	1065 (1021-1110)	--	1.5	--
WR 2721	741	871	--	*	--	*	--	*	--	*
WR 44923	517	--	*	--	*	--	*	--	*	--
WR 109342	24.9	38.8	--	*	--	*	--	*	--	*
WR 151327	677	--	*	--	*	--	*	--	*	--
WR 176542	434	--	*	--	*	--	*	--	*	--

TABLE II

Lethality - Co-60

DRUG	i.p. Dose (mg/kg)	LD50(6)* (RADS)	LD50(6) DMF	LD50(30)* (RADS)	LD50(30) DMF
None	--	252(239-266)	--	220	--
WR 347	220	350(336-365)	1.39	268	1.22
WR 2721	741	318(304-329)	1.26	267	1.21
WR 3689	970	337	1.34	334	1.52
WR 44923	517	337	1.34	305	1.39
WR 151327	677	358	1.42	319	1.45
WR 168643	852	313	1.24	267	1.67
WR 176542	434	311	1.23	260	1.18

TABLE III

Lethality - Neutrons

*Values in parentheses are 95% confidence limits; where no confidence limits appear the LD50 was estimated by linear regression.

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NUCLEAR DIVISION

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June 25, 1981

Dr. C. P. Sigdestad
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Radiation Center
Department of Therapeutic Radiology
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Louisville, Kentucky 40292

Dear Curt:

On June 10, 1981, Dr. Mike Conner picked up his ORNL "intermittent" badge which is valid for one year (yours is available too) and brought 210 mice to the DOSAR facility. The mice were stored in the air conditioned building number 7712. The drugs to be tested for their radioprotective effects (i.e., MEA and WR 2721) were taken from an ice chest and stored in a refrigerator in Building 7710.

On June 11 and 12, the mice were divided into groups and irradiated during six separate HPRR runs. All 210 mice were irradiated: 70 were "controls," 70 were injected with MEA, and 70 were injected with WR 2721. All reactor runs were made at a power of 2 kW, but the different doses were obtained by varying the run times and distances from the HPRR. The actual neutron dose was determined by sulfur pellet analysis along with an adjustment for the experimental configuration (see below). The gamma dose in rads is approximately 15% of the neutron dose in rads. Table 1 is a listing of relevant experimental data.

The irradiations were performed with the animals inside 3.0 mm thick nylon tubes borrowed from Mark Jernigan of the ORNL Biology Division. On June 23, the DOSAR staff determined experimentally that the tubes reduce the unshielded neutron dose by a factor of 0.972 (Biology Division had not previously made such a test, but assumed no reduction due to the tubes). The factor of 0.972 is considered in the actual dose reported in Table 1. The neutron dose reported is kerma; the units are rads. Details of the DOSAR facility's reference dosimetry are presented in ORNL/TM-7748 which is in press and scheduled to be issued in July.

Sincerely,

C. S. Sims, Ph.D.
Health and Safety Research Division
Phone: (615) 574-5851

CSS:rod
cc: [redacted] R. T. Greene
D. E. Davidson, Jr. P. S. Rohwer
L. W. Gilley R. E. Swaja

Table 1. Experimental data

	Distance from HPRR, m	Neutron dose, rads target	Neutron dose, rads actual	No. of mice	Type of drug
		Run No. 1			
Date – 6/11/81	2.00	350	347	10	MEA
Drug injection	2.54	225	223	5	MEA
complete – 0939	2.91	175	173	10	None
Run start – 1013	3.17	150	148	5	None
Run duration – 672 sec					
S pellet – 3182H					
		Run No. 2			
Date – 6/11/81	2.00	250	249	10	MEA
Drug injection	2.00	250	249	5	WR 2721
complete – 1052	2.12	225	224	10	None
Run start – 1132	2.26	200	199	10	None
Run duration – 480 sec					
S pellet – 3183H					
		Run No. 3			
Date – 6/11/81	2.00	325	323	10	WR 2721
Drug injection	2.19	275	273	10	WR 2721
complete – 1257	2.19	275	273	10	MEA
Run start – 1338	2.30	250	249	10	None
Run duration – 624 sec					
S pellet – 3184H					
		Run No. 4			
Date – 6/11/81	2.00	325	323	10	MEA
Drug injection	2.09	300	297	10	WR 2721
complete – 1421	2.09	300	297	10	MEA
Run start – 1459	2.19	275	273	10	None
Run duration – 624 sec					
S pellet – 3185H					
		Run No. 5			
Date – 6/12/81	2.00	400	390	10	WR 2721
Drug injection	2.00	400	390	5	MEA
complete – 0838	2.07	375	366	10	MEA
Run start – 0916	2.33	300	294	10	None
Run duration – 768 sec					
S pellet – 3186H					

Table 1. (continued)

	Distance from HPRR, m	Neutron dose, rads target	Neutron dose, rads actual	No. of mice	Type of drug
		Run No. 6			
Date — 6/12/81	2.00	460	461	5	WR 2721
Drug injection	2.07	430	432	10	WR 2721
complete — 1009	2.32	350	350	10	WR 2721
Run start — 1041	2.41	325	326	5	None
Run duration — 883 sec					
S pellet — 3187H					

OAK RIDGE NATIONAL LABORATORY
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POST OFFICE BOX X
OAK RIDGE, TENNESSEE 37830

July 22, 1981

Dr. C. P. Sigdestad
University of Louisville
Radiation Center
Department of Therapeutic Radiology
500 South Floyd Street
Louisville, Kentucky 40292

Dear Curt:

On July 15, 1981, Dr. Mike Connor and Michael McWilliams delivered the experimental mice to Building 7712, stored the radioprotective drugs in Building 7710, discussed experimental details with me, and borrowed from Mark Jernigan the nylon tubes in which the mice were to be irradiated.

On July 16 and 17, the mice were divided into groups, given radioprotective drugs, and irradiated during eight separate HPRR runs. A total of 280 mice were irradiated to target neutron doses varying from 225 to 400 rads (see Table 1). This experiment involved five different radioprotective drugs: WR 3689, WR 44923, WR 151327, WR 168643, and WR 176542. Each drug was given to 56 mice (see Table 2). The eight HPRR runs were numbered 7-14; runs 1-6 were performed on June 11-12.

As before, all reactor runs were made at a power of 2 kW and the different doses were obtained by varying the run times and distances from the HPRR. The actual neutron doses were determined by sulfur pellet analysis with an adjustment factor of 0.972 to account for the dose reduction due to the nylon tubes. The actual neutron doses delivered to the mice were within 2% of the target doses for all cases and are presented in Table 3 along with other relevant experimental data. Measurements confirmed that the gamma dose in rads was approximately 15% of the neutron dose in rads.

Photographs of the mice being prepared for irradiation and of the experimental setup including the HPRR were taken on July 17. The two photographs and slides should be ready during your next visit to ORNL.

Sincerely,

Steve

C. S. Sims
Health and Safety Research Division
Ph: (615) 574-5851

CSS:rod
cc: [redacted] Conner
D. E. Davidson, Jr.
L. W. Gilley
R. T. Greene
P. S. Rohwer
R. E. Swaja

Table 1. Number of mice targeted to receive the specified neutron dose

Target neutron dose,* (rads)	Number of mice given dose
225	20
250	40
275	40
300	40
325	40
350	40
375	40
400	20
	280

*Actual doses were within 2% of the target doses for all irradiations (see Table 3).

Table 2. Drugs given to the mice

Run number	No. of mice	Number of mice given drug*				
		A	B	C	D	E
7	32	12	12	8	-	-
8	32	8	8	12	4	-
9	40	8	8	8	8	8
10	32	4	-	-	16	12
11	40	8	8	8	8	8
12	32	8	12	4	-	8
13	32	-	-	8	12	12
14	40	8	8	8	8	8
Totals	280	56	56	56	56	56

*Drug identification is as follows:

A = WR 3689
B = WR 44923
C = WR 151327
D = WR 168643
E = WR 176542

Table 3. Experimental data

Identifying items	Distance from HPRR, m	Neutron dose, rads		No. of groups of mice at distance	No. of mice in group* for a given type drug				
		Target	Actual		A	B	C	D	E
Run - 7 Operation - 2351 Date - 7/16/81 DIC† - 0842 Run start - 0930 Run duration - 480 sec S pellets - 3189 D&H	2.00	250	250	3	8	8	8	-	-
	2.12	225	225	2	4	4	-	-	-
Run - 8 Operation - 2351 Date - 7/16/81 DIC† - 1006 Run start - 1044 Run duration - 528 sec S pellets - 3190 D&H	2.00	275	274	3	8	8	8	-	-
	2.23	225	224	2	-	-	4	4	-
Run - 9 Operation - 2351 Date - 7/16/81 DIC† - 1109 Run start - 1153 Run duration - 576 sec S pellets - 3191 D&H	2.00	300	299	5	8	8	8	8	8

*A = WR 3689, B = WR 44923, C = WR 151327, D = WR 168643, E = WR 176542.

†DIC = time drug injection completed.

Table 3. (continued)

Identifying items	Distance from HPRR, m	Neutron dose, rads		No. of groups of mice at distance	No. of mice in group* for a given type drug				
		Target	Actual		A	B	C	D	E
Run - 10									
Operation - 2351	2.00	400	393	1	4	-	-	-	-
Date - 7/16/81	2.45	275	270	1	-	-	-	8	-
DIC† - 1321	2.58	250	245	2	-	-	-	8	8
Run start - 1357	2.73	225	221	1	-	-	-	-	4
Run duration - 768 sec									
S pellets - 3192 D&H									
Run - 11									
Operation - 2351									
Date - 7/16/81									
DIC† - 1434	2.00	325	324	5	8	8	8	8	8
Run start - 1515									
Run duration - 624 sec									
S pellets - 3193 D&H									
Run - 12									
Operation - 2352									
Date - 7/17/81	2.00	400	396	2	-	4	4	-	-
DIC† - 1000	2.15	350	346	2	8	8	-	-	-
Run start - 1042	2.45	275	272	1	-	-	-	-	8
Run duration - 768 sec									
S pellets - 3194 D&H									

*A = WR 3689, B = WR 44923, C = WR 151327, D = 168643, E = WR 176542.

†DIC = time drug injection completed.

Table 3. (continued)

Identifying items	Distance from HPRR, m	Neutron dose, rads		No. of groups of mice at distance	No. of mice in group* for a given type drug				
		Target	Actual		A	B	C	D	E
Run - 13 Operation - 2352 Date - 7/17/81 DIC† - 1115 Run start - 1145 Run duration - 768 sec S pellets - 3195 D&H	2.00	400	394	2	-	-	-	4	4
	2.15	350	344	3	-	-	8	8	8
Run - 14 Operation - 2352 Date - 7/17/81 DIC† - 1220 Run start - 1249 Run duration - 720 sec S pellets - 3196 D&H	2.00	375	375	5	8	8	8	8	8

*A = WR 3689, B = WR 44923, C = WR 151327, D = WR 168643, E = WR 176542.

†DIC = time drug injection completed.

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20. ABSTRACT (Continue on reverse side if necessary and identify by block number)

This report deals with the assays of various compounds for their toxicity of anti-radiation efficacy following exposure to either Co-60 or fission neutron irradiation. The compounds reported herein include WR 347, WR 2721, WR 3689, WR 44923, WR 109342, WR 151327, WR 16843, and WR 176542. The endpoints measured in the radiation studies were LD50(6) and LD50(30). —> cont

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20. Abstract (continued)

The compounds and their dose modification factors (DMF) for the neutron LD50(6) following i.p. administration, were, in descending order of effectiveness: WR 151327 (1.42), WR 347 (1.37), WR 3689 (1.34) WR 44923 (1.34), WR 2721 (1.26), WR 168643 (1.24), and WR 176542 (1.23). The corresponding LD50(30)'s for fission neutron irradiation following i.p. administration, were: WR 168643 (1.67), WR 3689 (1.52), WR 151327 (1.45), WR 44923 (1.39), WR 347 (1.22), WR 2721 (1.21), and WR 176542 (1.18).

For low LET Co-60 gamma irradiation the LD50(6) and LD50(30) were determined for WR 347 following i.p. administration. The DMF's obtained were: LD50(6) (1.4), LD50(30) (1.5).


DATE
ILME